

Bone Health Monitoring in Astronauts: Recommended Use of Quantitative Computed Tomography [QCT] for Clinical and Operational Decisions

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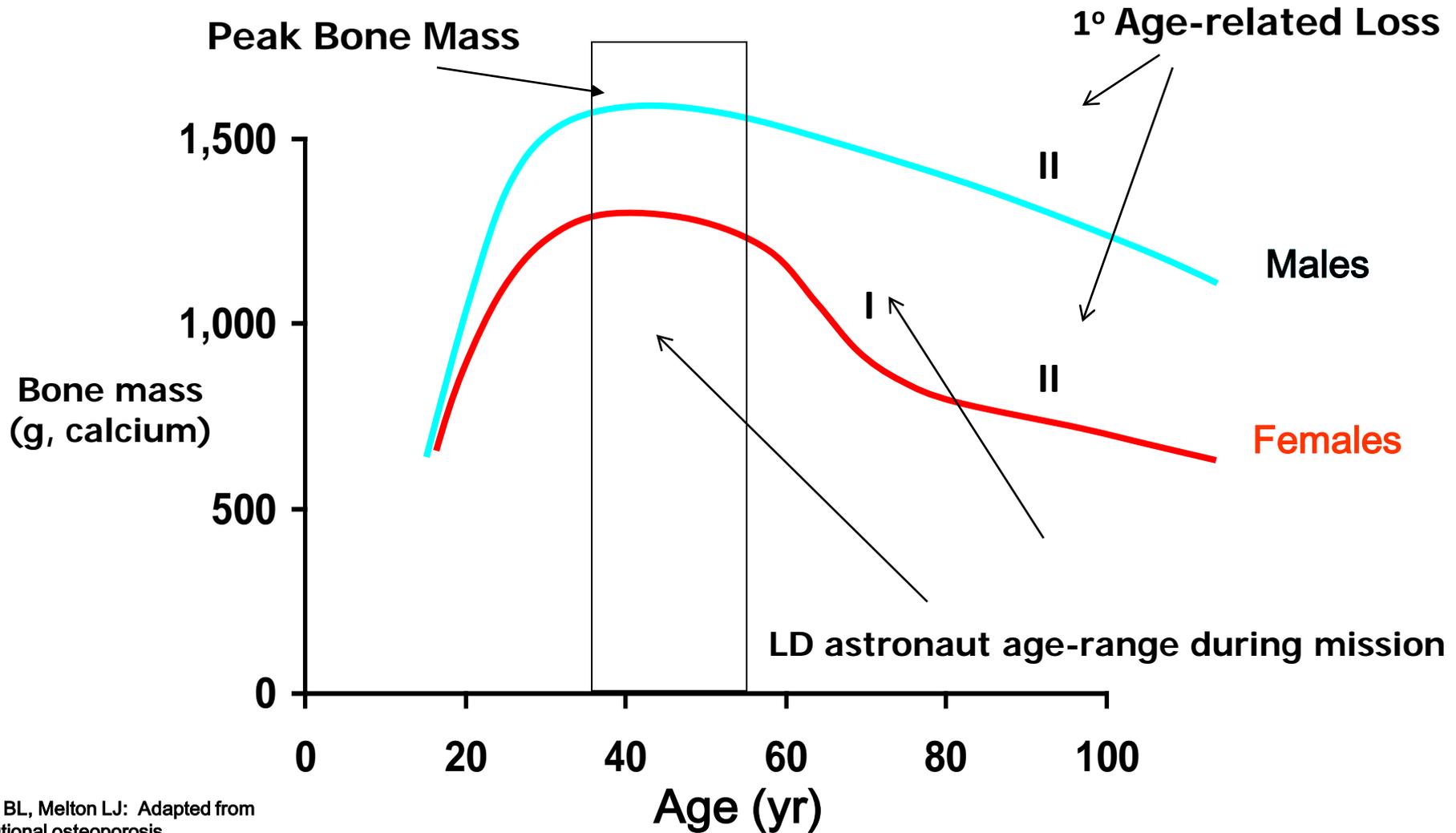
On behalf of the NASA Bone Summit Panel for
Early Onset Osteoporosis in Long-Duration Astronauts.

June 7-8, 2010

Houston, TX

BASIS FOR BONE SUMMIT

Does spaceflight induce enduring changes to bone that combine with age-related losses?

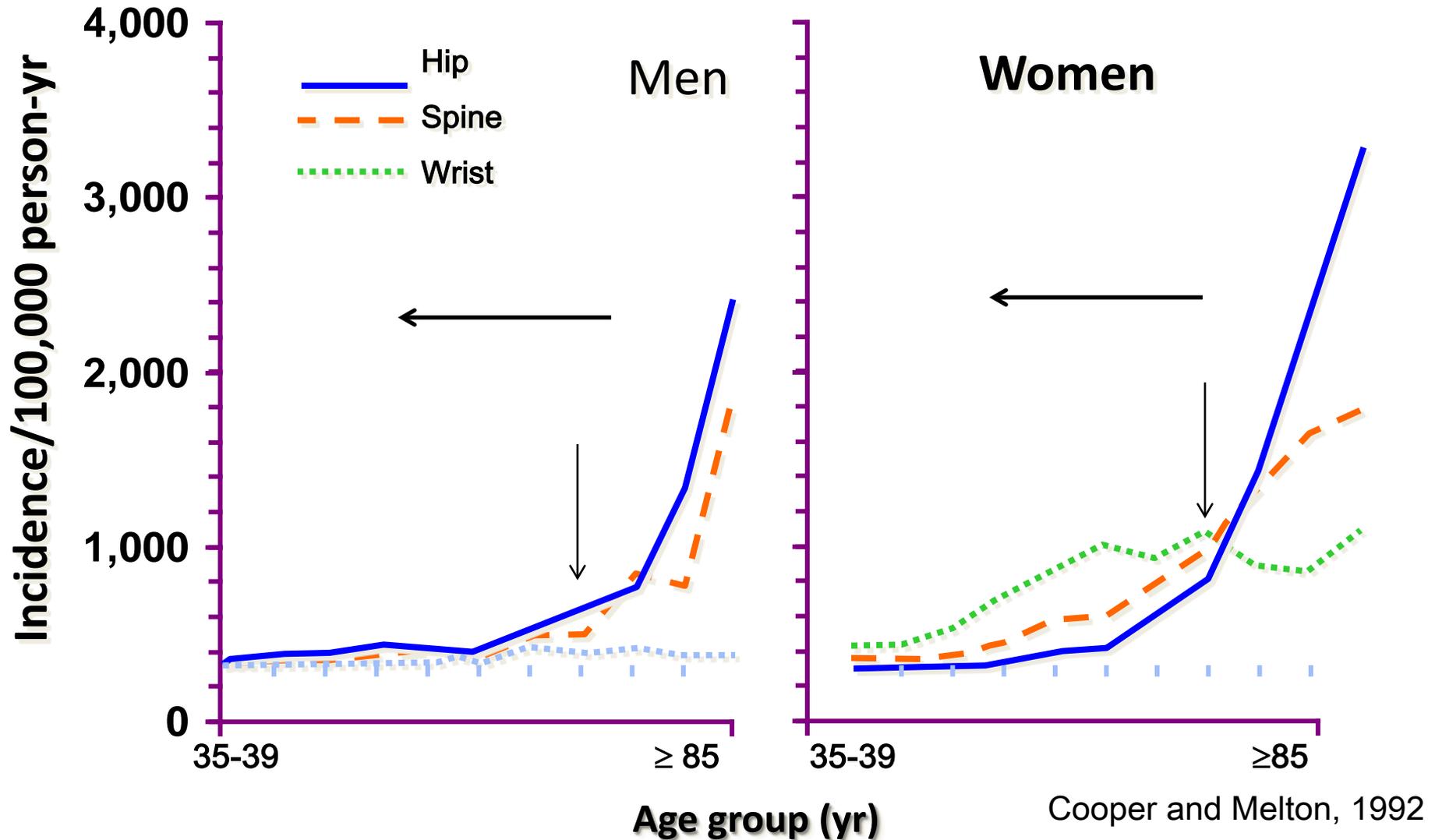


Riggs BL, Melton LJ: Adapted from
Involutional osteoporosis
Oxford Textbook of Geriatric Medicine

Slide courtesy of Amin adapted by Sibonga



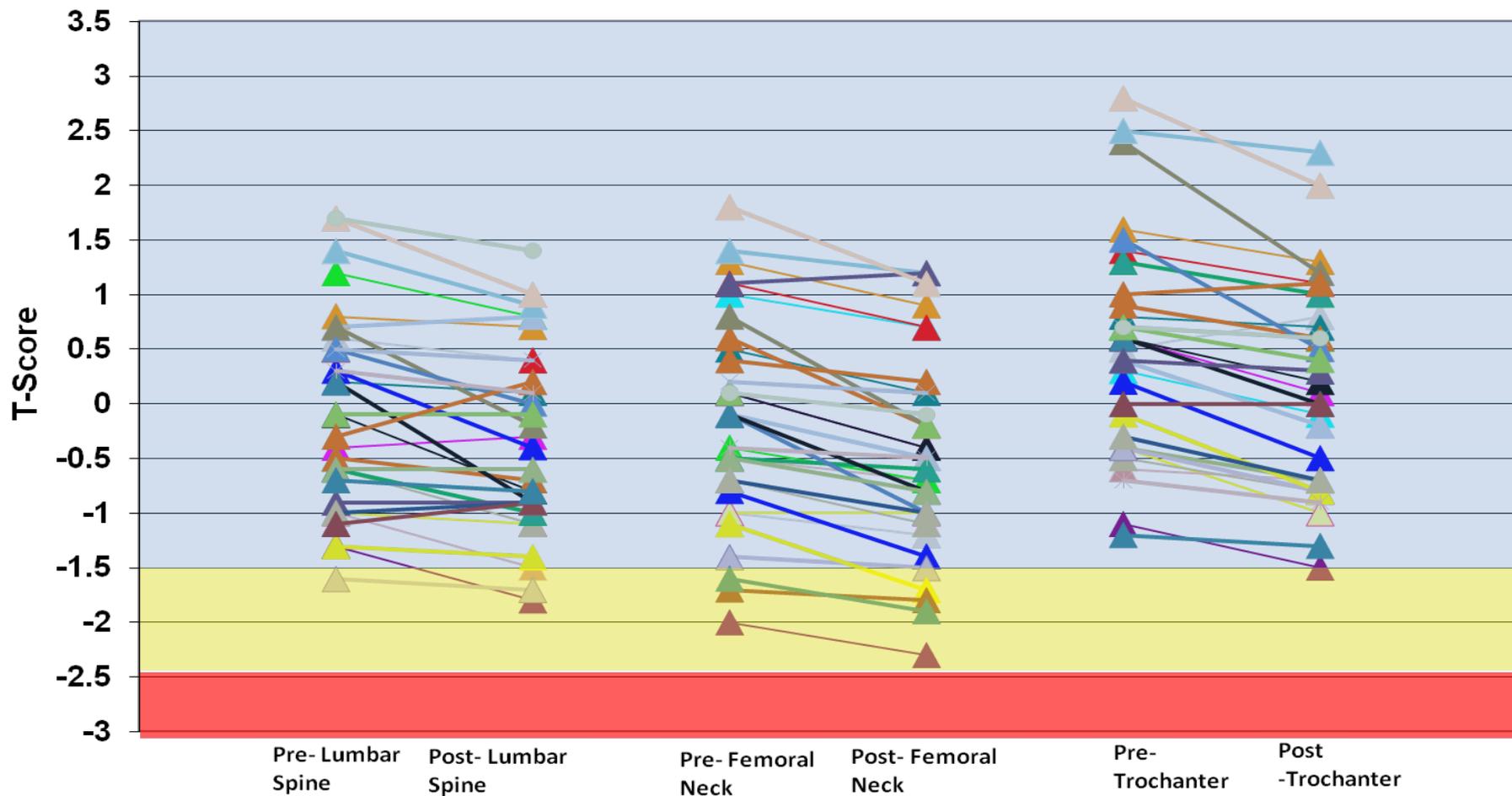
Risk: Do age-related fractures occur prematurely due to previous exposure to long-duration spaceflight.



To-date, subclinical effect, but T-scores are inappropriate and not informative for long-duration astronauts

BMD T-Score Values* Expeditions 1-25 (n=33)

*Comparison to Population Normals



Clinical Significance: Impact of Age-related Hip Fractures

- 50% of survivors post-hip fracture require institutional care or functional assistance
- Decreased quality of life and negative health outcomes for men and women with vertebral deformity *Poor Osteoporosis Intl. 1995; Matthis Osteoporosis Intl. 1998; Scane Osteoporosis Intl. 1999*

MEN TEND TO DO WORSE

- Twice as likely to die in hospital following hip fracture than women
- 1 year mortality rate following hip fracture is higher compared with women (31-35% vs. 17-22%) *Myers, Am J Epi 1991, Schurch JBMR 1996, Forsen Osteoporosis Intl. 1999, Kiebzak Arch Int Med 2002*

Notably, spaceflight-induced skeletal changes could also impact fracture risk **after** return to earth if recovery of bone strength is not sufficiently established.

- In the post-mission period when the LD astronaut returns to preflight level of physical activity
- In the aging astronaut before or concurrent with age-related bone loss.*

* age-related bone loss is sex-specific (see figure) with females losing bone mass earlier with the onset of menopause.

Given the **following**, it becomes more critical to reduce the uncertainty with how bone mass and bone structure change due to spaceflight and with recovery on earth after a mission.

*“An **asymptomatic** systemic bone disease characterized by low bone mass and **microarchitectural deterioration** of bone tissue, with a consequent increase in bone fragility and susceptibility of fracture”*

Am J Med 1993; Consensus Development Conference: diagnosis, prophylaxis and treatment of osteoporosis

*“Bone strength reflects the integration of two main features: bone density and **bone quality**.”*

JAMA, 2001

*“...Bone quality, in turn, is stated to refer to **architecture, turnover, damage accumulation, (e.g., microfractures) and mineralization....**”*

Osteoporosis Intl. 2002

“Bone Quality: What is it and Can we measure it?”

Focused ASBMR- NIH Forum, May 2005

*“**Structural determinants** of vertebral fracture risk.”*

Melton et al. J Bone Mineral Research, 2007

But, how does Space Medicine use emerging research technologies and data in clinical practice?

Action to convene a panel of clinical experts for a Bone Summit on Early Onset Osteoporosis in Long-Duration Astronauts.

Bone Summit Panel will be asked to:

- **Consider the Cohort:** Long-duration Astronauts- not the typical target population for evaluating osteoporosis or for determining age-related fracture risk.
- **Understand the Constraints:** NASA has a limited and insufficient dataset to describe the multi-factorial effects of prolonged spaceflight (small n, limited technologies, restricted data collection).
- **Recommend a Therapeutic Course of Action:** Panelists need to be leaders in the field of bone, knowledgeable in densitometry data and bone loss risk factors
- **Recommend Approaches for Occupational Risk Surveillance:** what should NASA do *now* to address an occupational health risk that may manifest *later*?



Bone Summit Panel Members



- Eric Orwoll, MD
 - Endocrinology and Male Osteoporosis
- E. Michael Lewiecki, MD, FACP, FACE
 - Endocrinology, ISCD
- Neil Binkley, MD, CCD
 - ISCD, Geriatrics and Vitamin D
- Shreyasee Amin, MD
 - Rheumatology, Male Osteoporosis and Epidemiology
- Sue Shapses, PhD
 - Nutritional Sciences and Weight-loss
- Robert A. Adler, MD
 - Male Osteoporosis and Epidemiology
- Steven Petak, MD, JD, FACE
 - Endocrinology, ISCD (contracted by )
- Mehrsheed Sinaki, MD
 - Physical Medicine & Rehabilitation
- Nelson B. Watts, MD
 - Endocrinology, ISCD

Insert photo

Left to Right, Top Row down

Summit Format and Charge to Panel*

Individual “charts” of operational & medical data were compiled from a subset of LD-astronauts representing novel scenarios or skeletal responses (females, repeat fliers, ARED users, with QCT data, with bone strength data, with > 10% loss in hip or spine). Following this critical review, the panel was asked to address the following charge:

- Can a **clinical trigger** be identified, from the evidence-to-date. that would require medical response and/or a possible intervention to prevent early onset osteoporosis?
- For occupational risk surveillance, recommend skeletal measures for monitoring the risk for premature age-related fractures in this population.

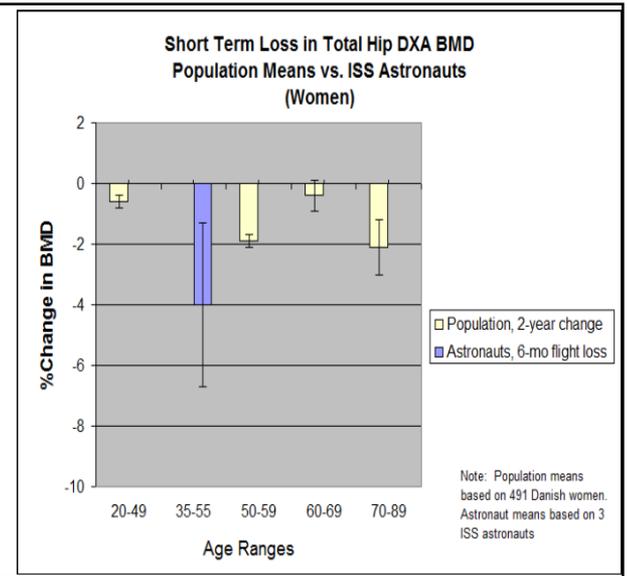
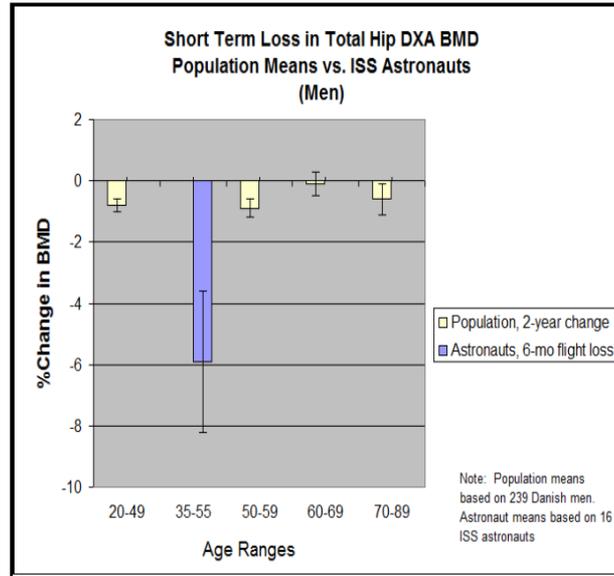
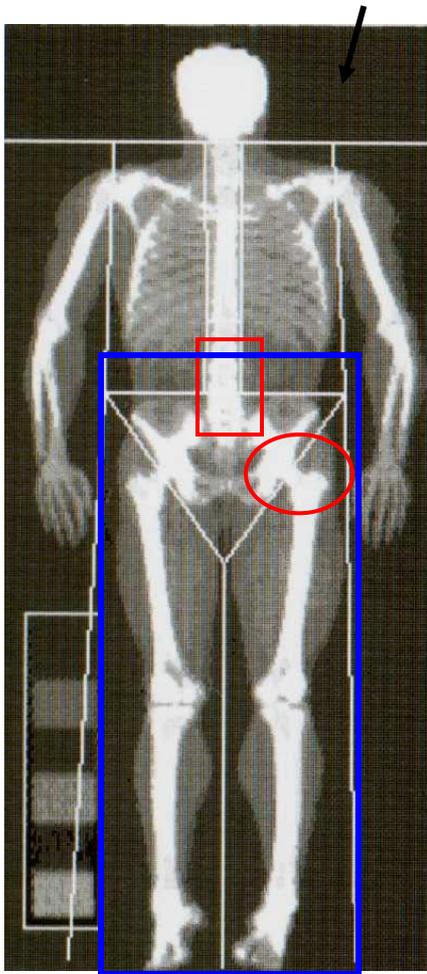
* Abbreviated for the theme of this IAA presentation

Flight and Earth-based Population Studies

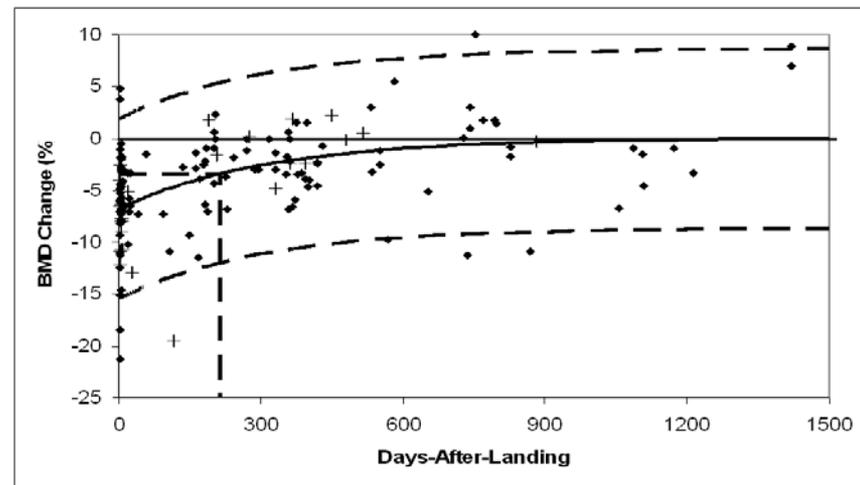
DATA BACKGROUND

DXA BMD Summary

Rapid (1-1.5%/mo) and site-specific BMD loss (local not metabolic).



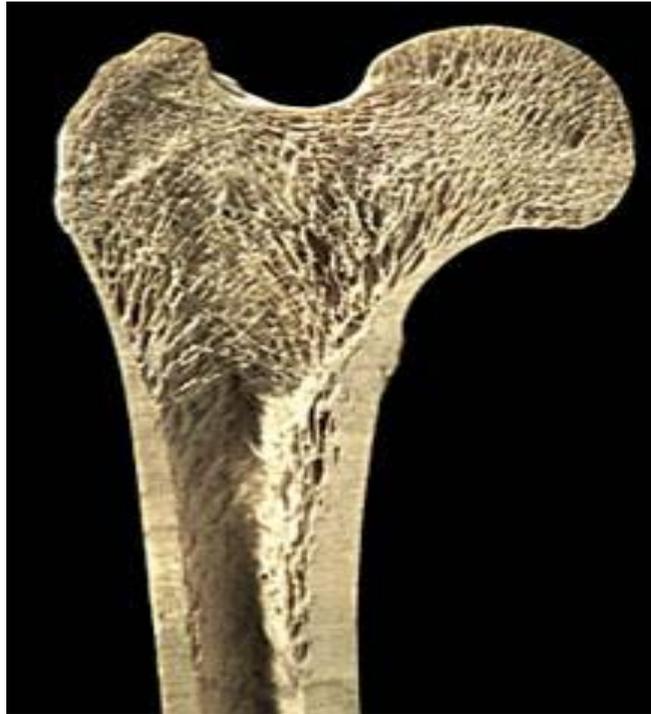
↗ Total BMD loss over 6 mo mission > 2 y loss in sex- and age-matched population on earth



↘ Loss is variable.
Recovery is variable.
Recovery is prolonged.
Indicates: Multiple Risk Factors at play.

QCT measures loss vBMD in trabecular bone compartment which DXA technology cannot (n=16 ISS)

NOT detectable by DXA

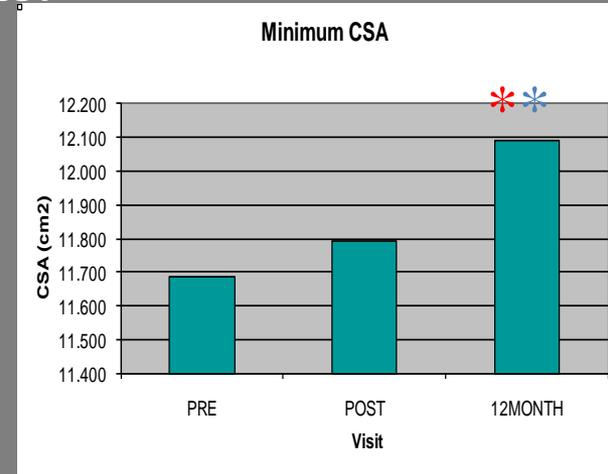
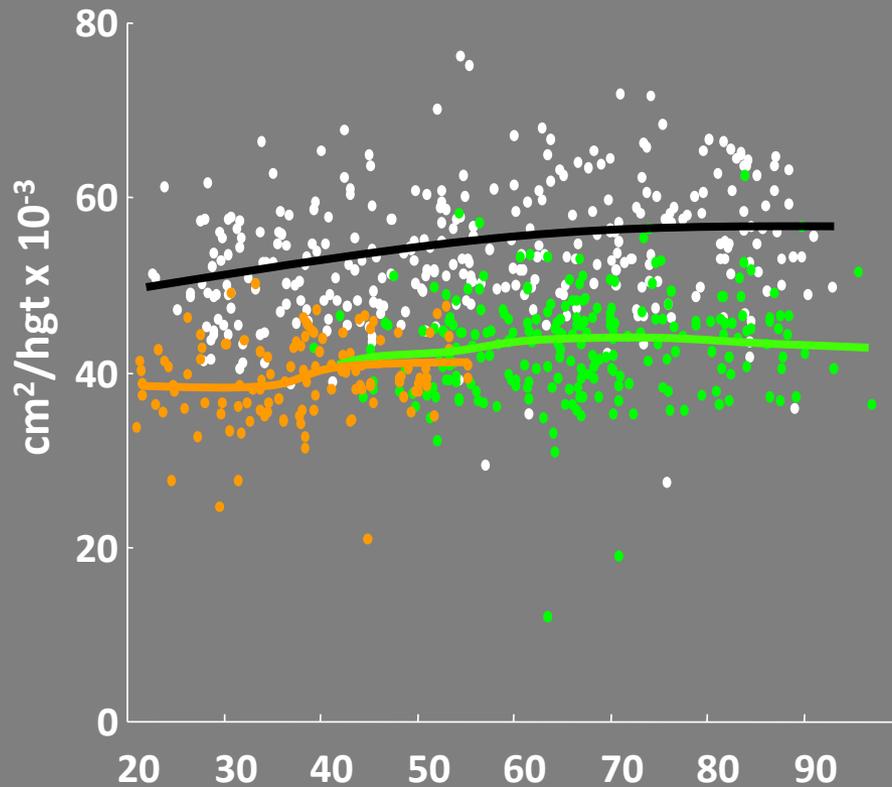


Index DXA	%/Month Change \pm SD	Index QCT	%/Month Change \pm SD
aBMD Lumbar Spine	1.06 \pm 0.63*	Integral vBMD Lumbar Spine	0.9 \pm 0.5
		Trabecular vBMD Lumbar Spine	0.7 \pm 0.6
aBMD Femoral Neck	1.15 \pm 0.84*	Integral vBMD Femoral Neck	1.2 \pm 0.7
		Trabecular vBMD Femoral Neck	2.7 \pm 1.9
aBMD Trochanter	1.56 \pm 0.99*	Integral vBMD Trochanter	1.5 \pm 0.9
*p<0.01, n=16-18		Trabecular vBMD Trochanter	2.2 \pm 0.9

LeBlanc, J M Neuron Interact, 2000;
Lang, J Bone Miner Res, 2004;
Vico, The Lancet 2000

QCT in Population Study and in Astronauts

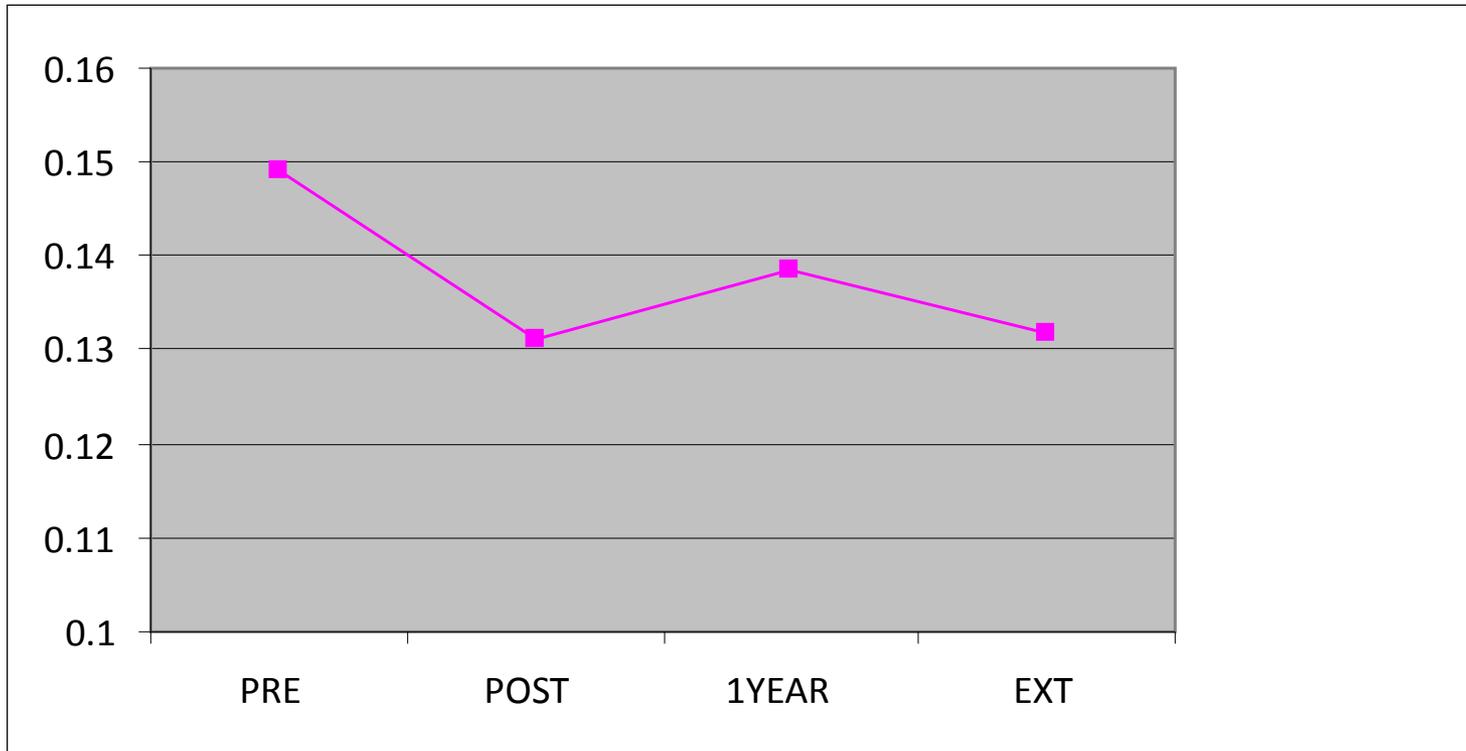
Suggests that femoral neck total area increases by outward displacement when cortex thins with aging— risk of space effects combining with aging effects.



Lang et al, JBMR, 2006

- Men
- Premenopausal women
- Postmenopausal women

QCT: Trabecular BMD at hip does not appear to show a recovery 2-4 years postflight.



PRE: n= 16 POST: n= 16 1 YEAR: n=16 EXT: n=8

QCT Extension Study (n=8) Postflight Trabecular BMD in hip. Carpenter, D et al. Acta Astronautica, 2010.

What is the impact of Trabecular Bone Loss on whole hip bone strength?

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Proximal Femoral Structure and the Prediction of Hip Fracture in Men: A Large Prospective Study Using QCT*

Dennis M Black,¹ Mary L Bouxsein,² Lynn M Marshall,³ Steven R Cummings,⁴ Thomas F Lang,⁵ Jane A Cauley,⁶ Kristine E Ensrud,⁷ Carrie M Nielson³ and Eric S Orwoll³ for the Osteoporotic Fractures in Men (MrOS) Research Group

Results: Lower trabecular BMD is an independent predictor of hip fracture in elderly men.

Overall, QCT measures provide useful information regarding causation of hip fracture, evaluation of hip fracture risk and possible targets for intervention.

Panel reviewed

EXPERT PANEL RECOMMENDATIONS

Recommended Clinical Trigger in Astronauts

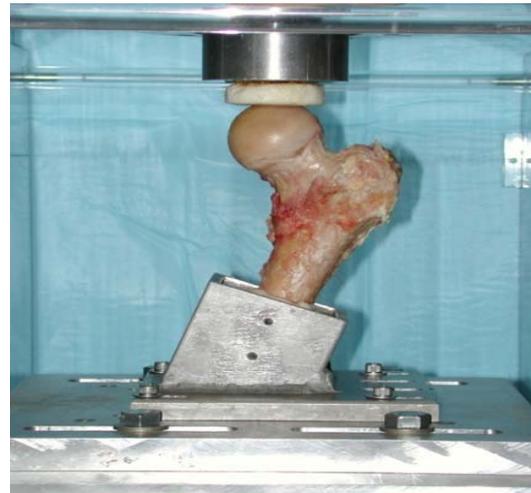
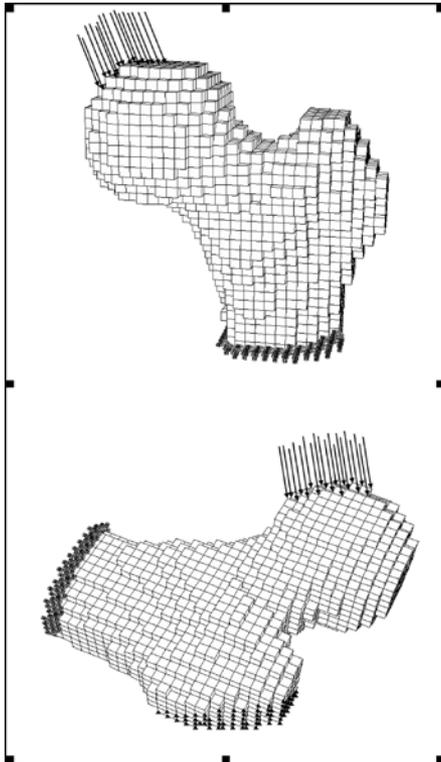
- **Recommended Postflight Clinical Trigger:** lack of recovery in trabecular compartment of hip at R+ 2 years (**regardless of DXA T-score**). Astronaut/flight doc seeks consult with endocrinologist (Petak) for evaluation and possible recommendation for intervention
- **Rationale:** Concern for irreversible deficits to this bone compartment – an independent fracture predictor.

QCT scans for Occupational Risk Surveillance

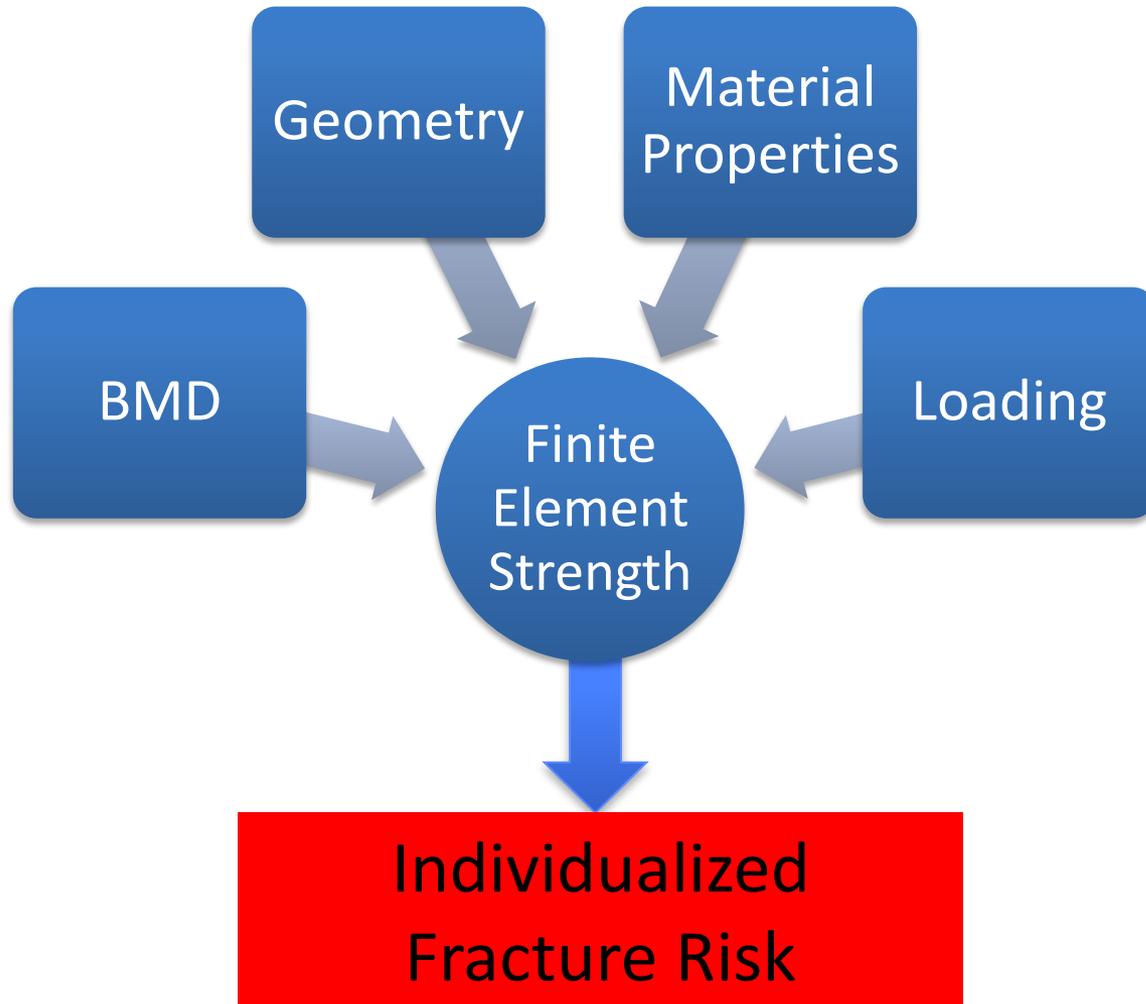
NASA's constraints may be the circumstances in which “research technologies should be transition to clinical realm.”

- **Required to detect clinical trigger** and for Countermeasure Evaluation: **clinical trigger based upon trabecular bone compartment** – not detectable by DXA but by QCT
- QCT's **additional** measures **reduce the uncertainty for fracture risk and for countermeasure efficacy**
- Added benefits: facilitates **individualized estimations of bone strength** by Finite Element Modeling (preliminary findings exist in flight evidence base). Can inform rehabilitation approaches.

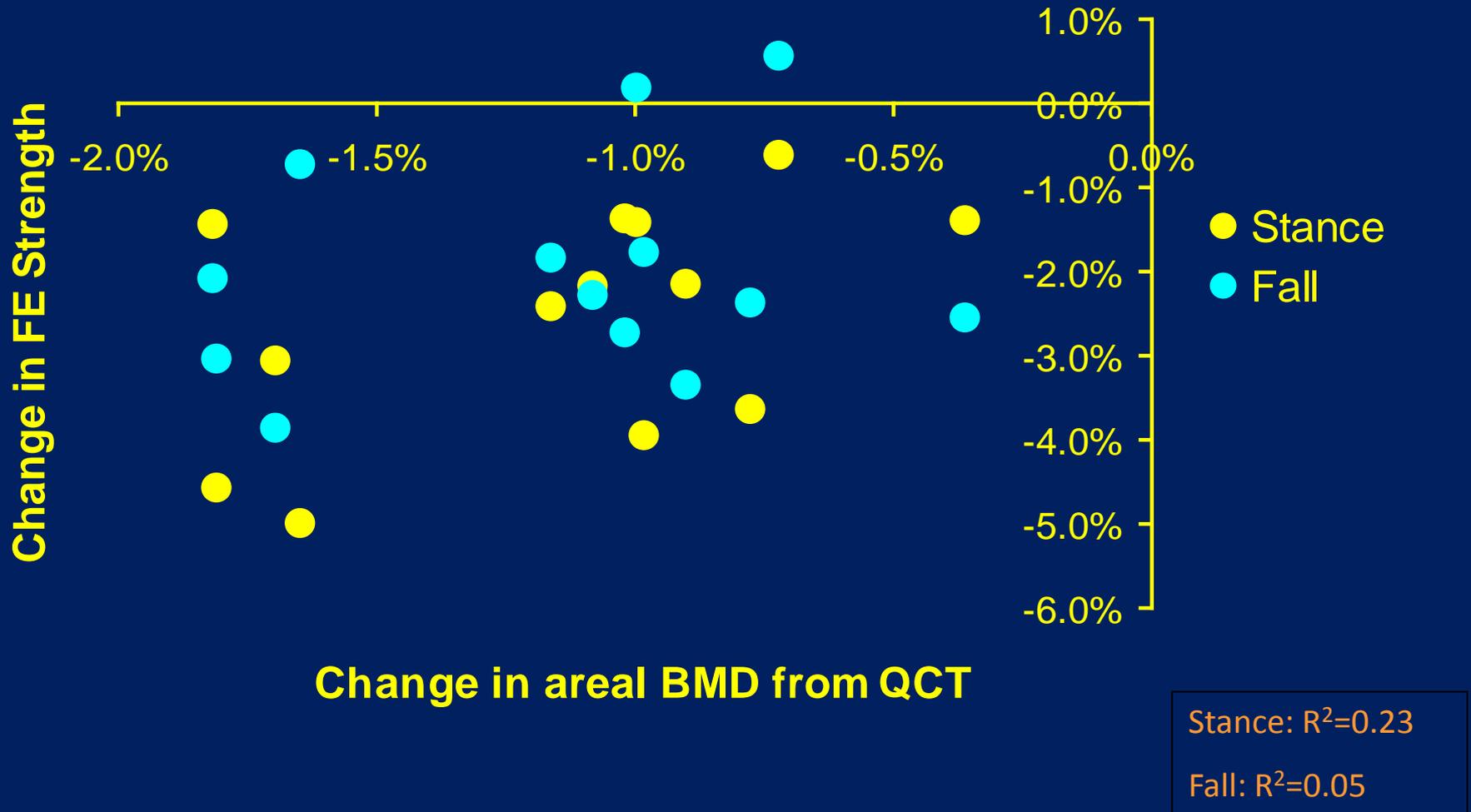
Why Apply Finite Element Modeling [FEM] to QCT data (a computational tool for complex structures) to assess failure loads of whole hip bone.



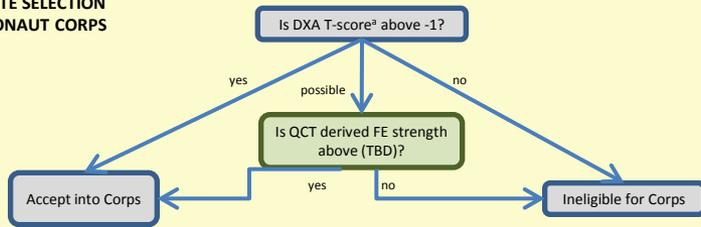
FEM may provide single best composite number to estimate bone strength because it integrates multiple factors.



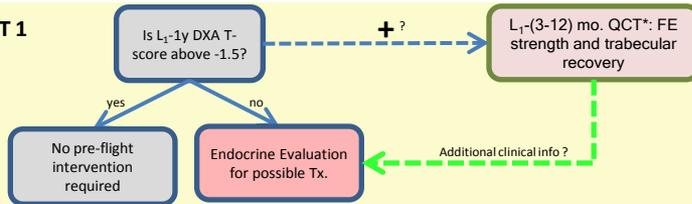
Astronaut data: surrogates of bone strength do not correlate suggesting that FEM can detect changes due to space that DXA surrogate cannot.



CANDIDATE SELECTION TO ASTRONAUT CORPS

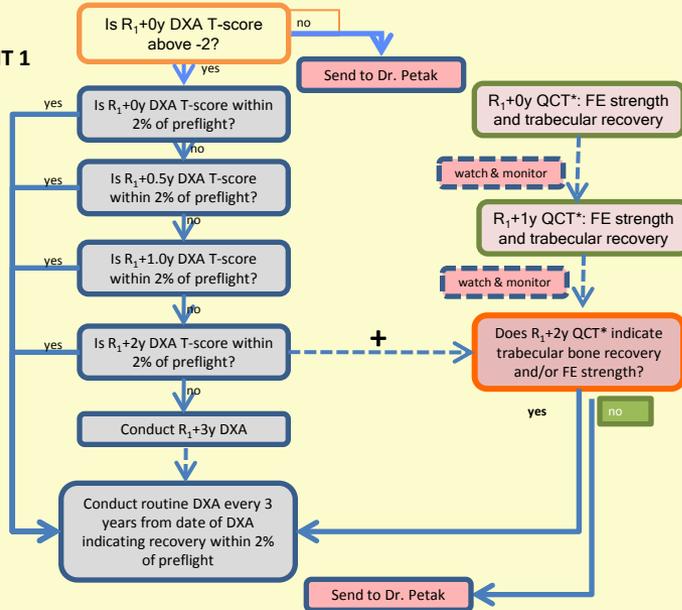


PRE-FLIGHT 1



Flight 1

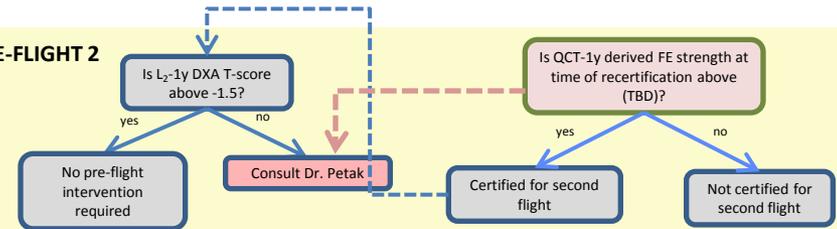
POST-FLIGHT 1



Use of QCT Technology for Clinical and Operational Decisions

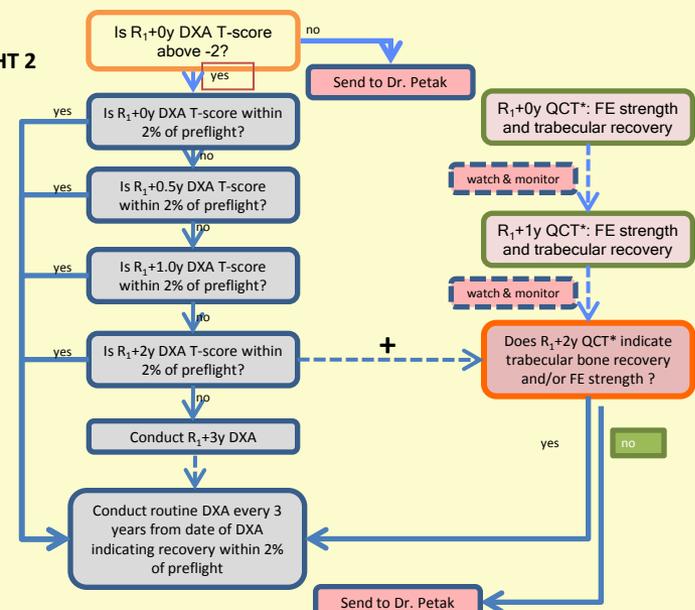
Recommendations from an Expert Panel for Consideration by NASA

PRE-FLIGHT 2



Flight 2

POST-FLIGHT 2



*All designated QCT scans are for occupational surveillance purposes.
 •a: Total Hip, Femoral Neck, Trochanter

Discussion

- NASA has a responsibility for the health of astronauts.
- QCT Surveillance will enable the collection of scientific knowledge, especially for measures that have been **validated in population studies**.
- QCT will increase the evaluation of bone changes due to space and with aging to address risks for current and future missions **and** risks to long-term health.
- Criticality to reduce uncertainty: Federal Employee Workman's Compensation requires a 3-5 year window to establish causality between occupational hazard and injury or disease.

Concluding Comments

How much uncertainty is acceptable to manage the skeletal risks for early onset osteoporosis and for bone fracture?

Increased **understanding** of spaceflight effects on bone by the Space Life Sciences Directorate:

- Will better inform decision-making (both clinical and operational),
- Will help direct focused and efficient countermeasure research and validation,
- Will improve the delineation of spaceflight causality substantiating occupational risk or injury,
- May lead to the translation of research technologies to earth-based medicine.